

VE-PTH-ONTO



NIKKOL VF-LINO (*INCI: ETHYL LINOLEATE*)

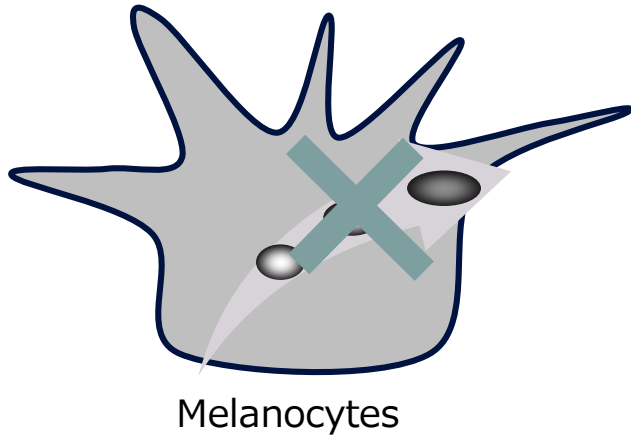
- **Palm free ! (Safflower Oil)**
- **Vitamin F (ω -6 essential FA's)**
- **China INCI**
- **QD additive in Japan**



Strategy of NIKKOL VF-LINO

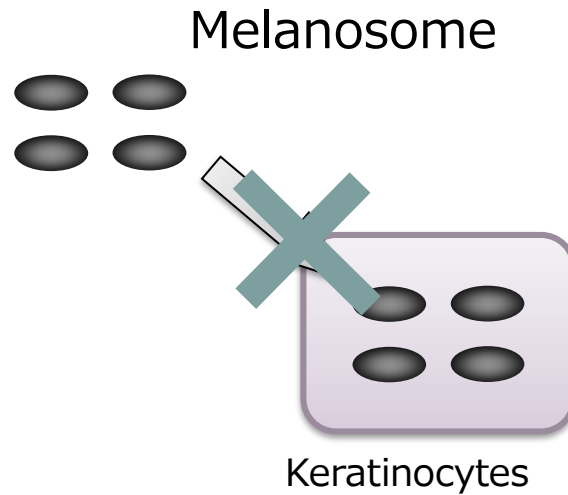
STEP1

Suppression of
melanin
production



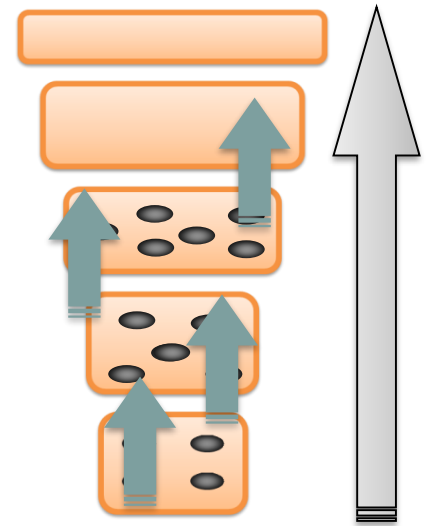
STEP2

Inhibition of
melanosome
uptake



STEP3

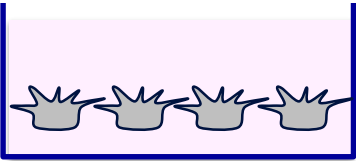
Turnover
promotion of
melanosome
Accumulated cell



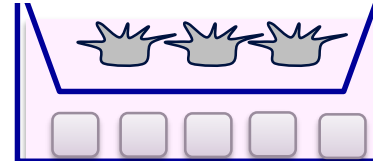
In vitro test

STEP1: Inhibition of melanin production

NHEMs: Normal Human Epidermal Melanocytes
NHEKs: Normal Human Epidermal Keratinocytes

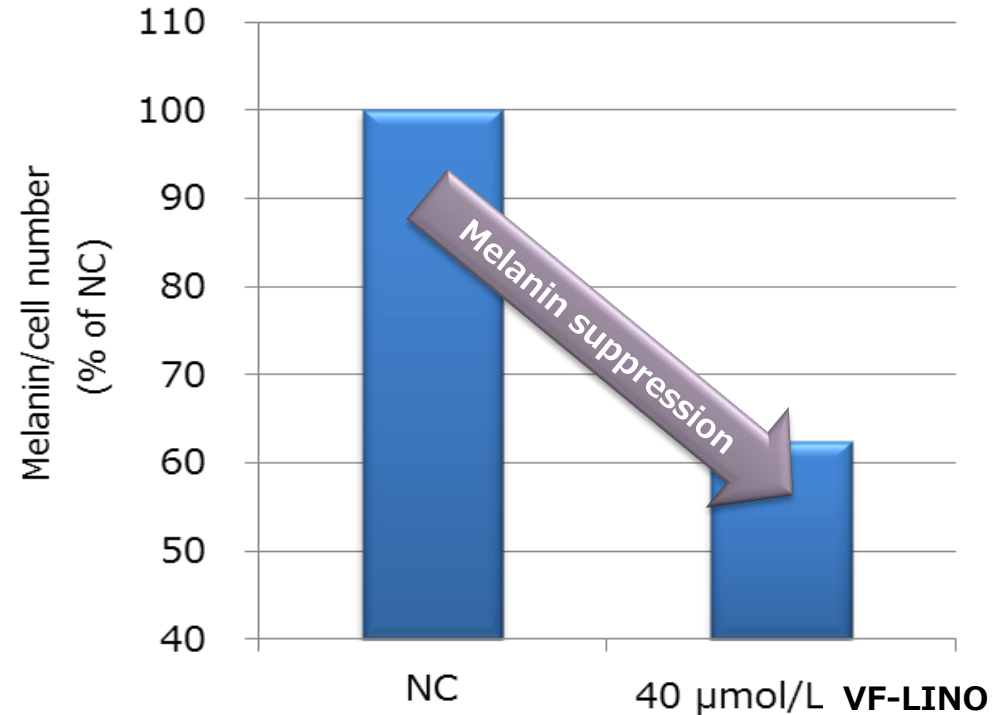
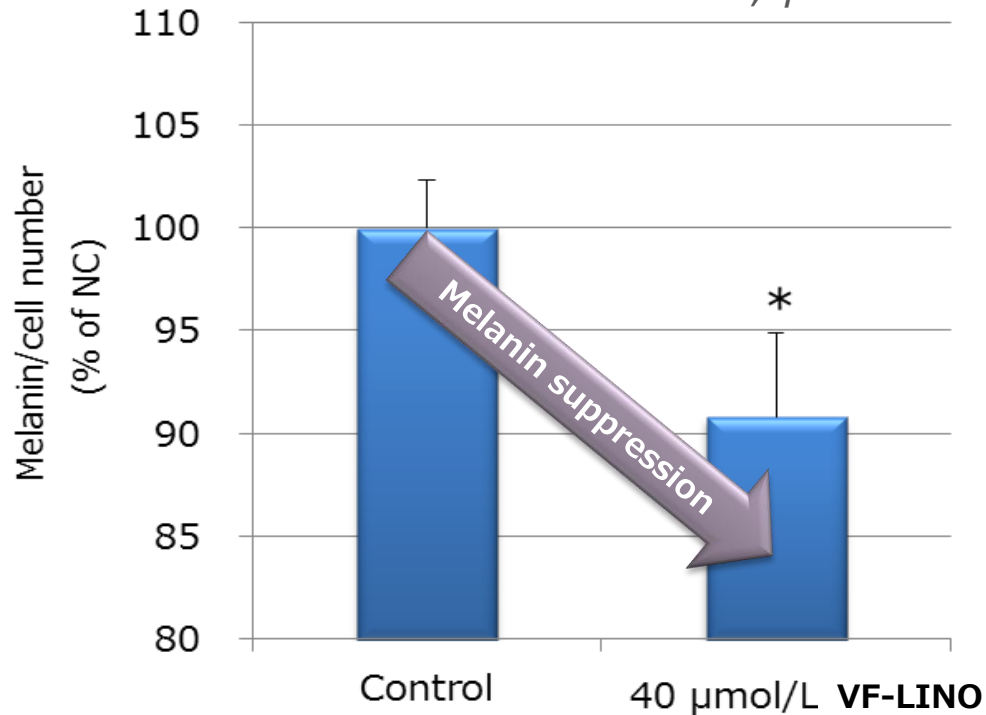


**Melanin
in NHEMs**



**Melanin
in NHEMs-NHEKs**

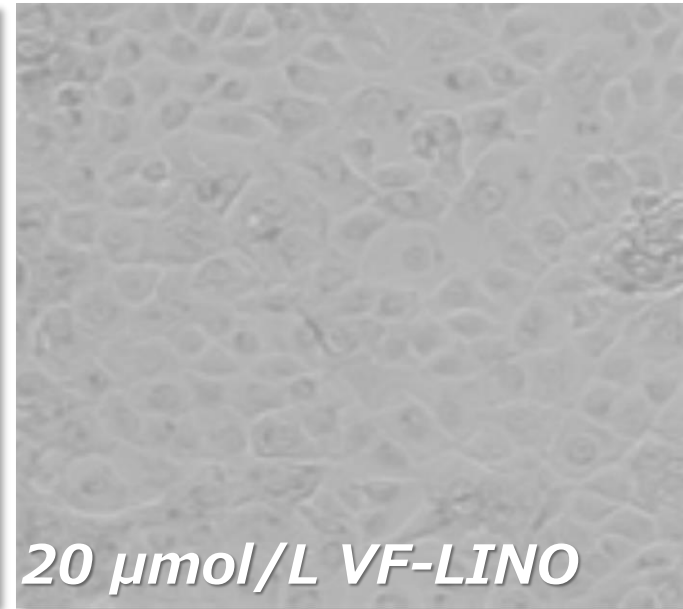
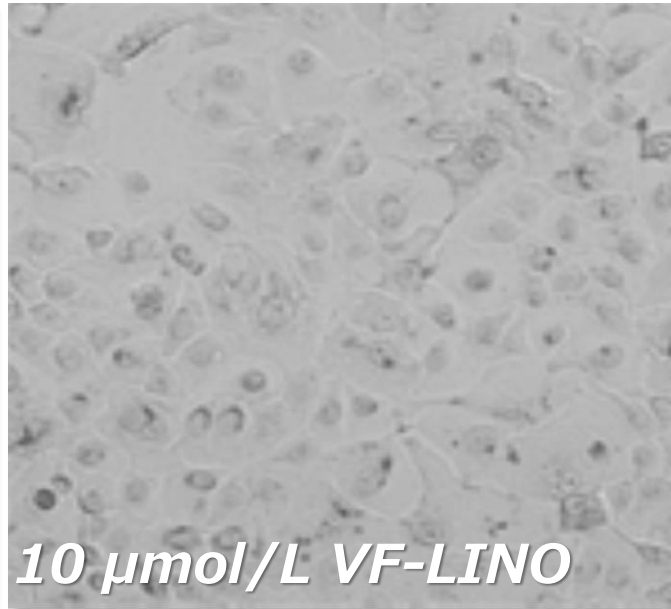
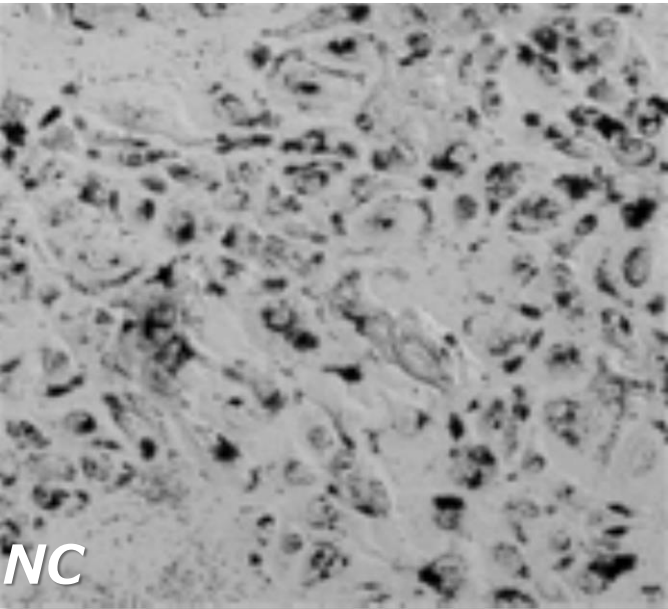
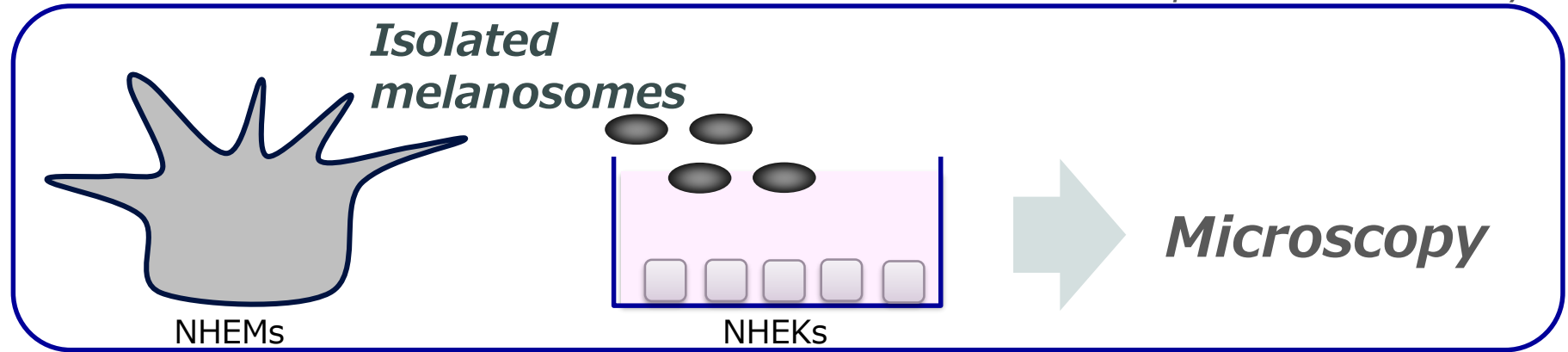
Student *t*-test; $p^* < 0.05$



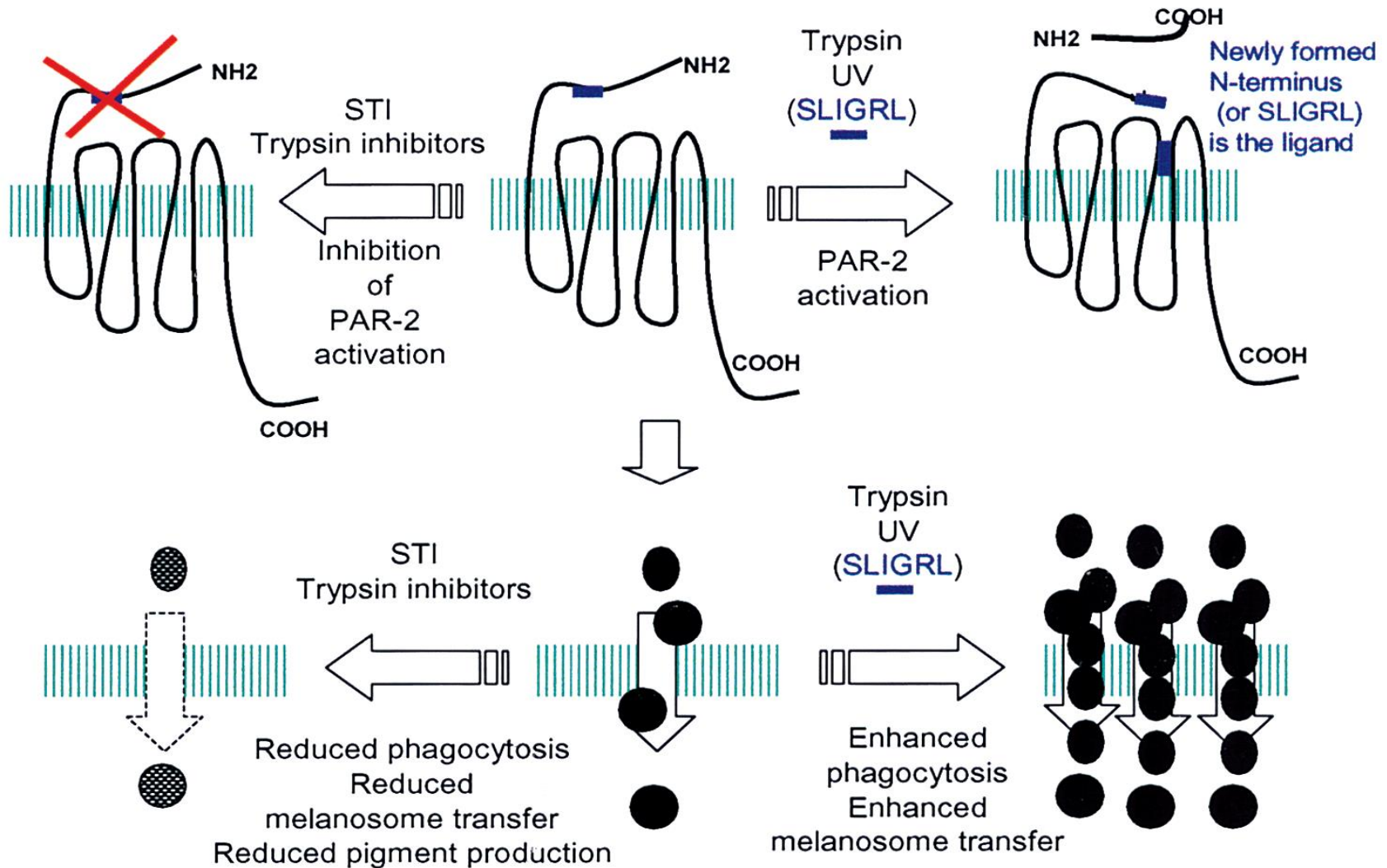
STEP2: Inhibition of melanosome uptake

NHEMs: Normal Human Epidermal Melanocytes

NHEKs: Normal Human Epidermal Keratinocytes



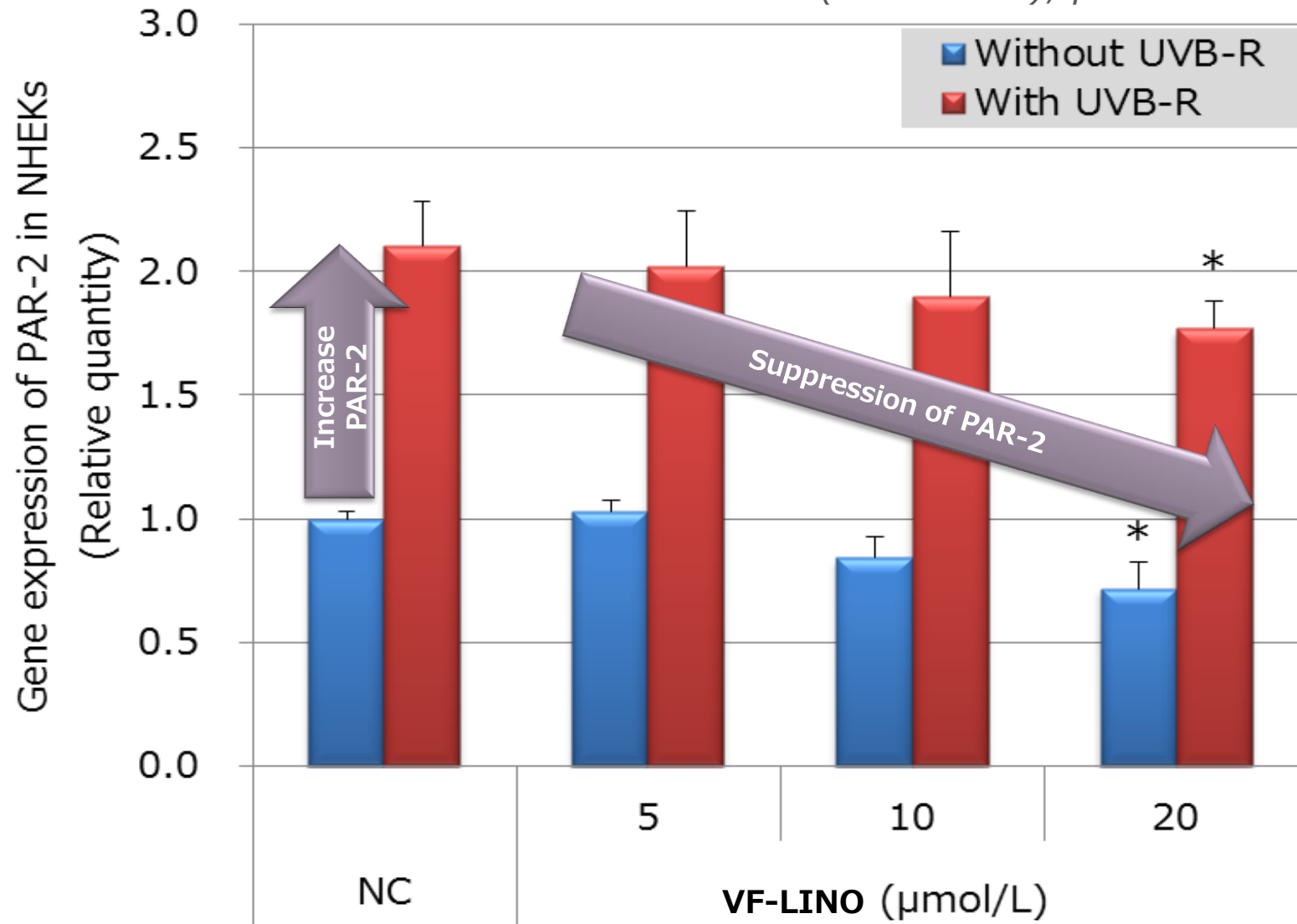
STEP2: Inhibition of melanosome uptake



Seiberg M. et al. *Pigment Cell Res.* 14: 236-242, 2001

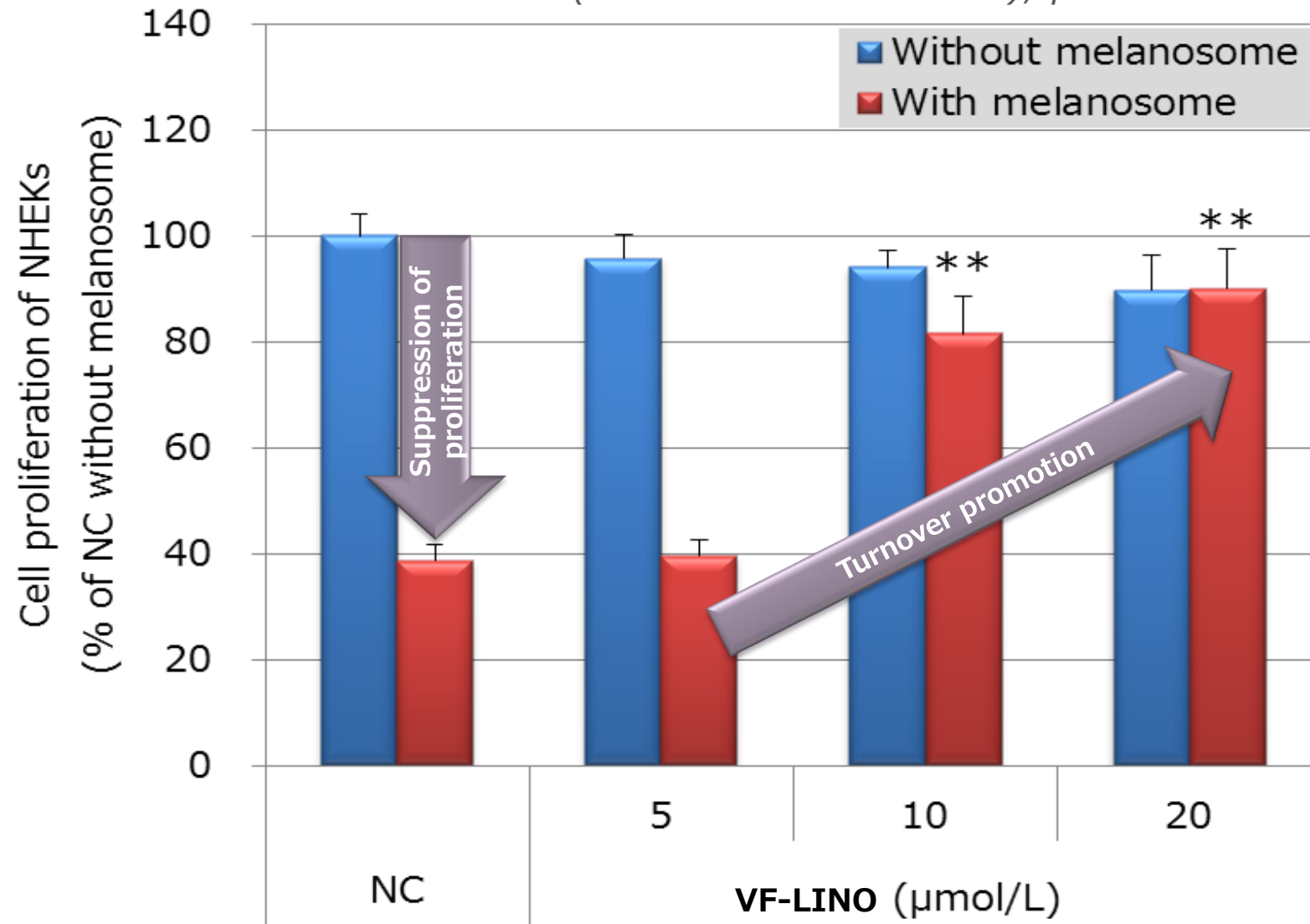
STEP2: Inhibition of melanosome uptake

*Student t-test(vs each NC); $p^{**}<0.05$*



STEP3: Turnover promotion

Student t-test(vs NC with melanosome); $p^{**}<0.05$



VE-PTH-ONTO



Why **VF-LINO** is effective for **PIH**?

PIH; Post Inflammatory Hyperpigmentation

Previous reports said...

- ✓ **Fatty acids such as linoleic acid regulated skin pigmentation via proteasomal degradation of tyrosinase.**

Fatty acids regulate pigmentation via proteasomal degradation of tyrosinase: a new aspect of ubiquitin-proteasome function.

J Biol Chem. 2004 Apr 9;279(15):15427-33.

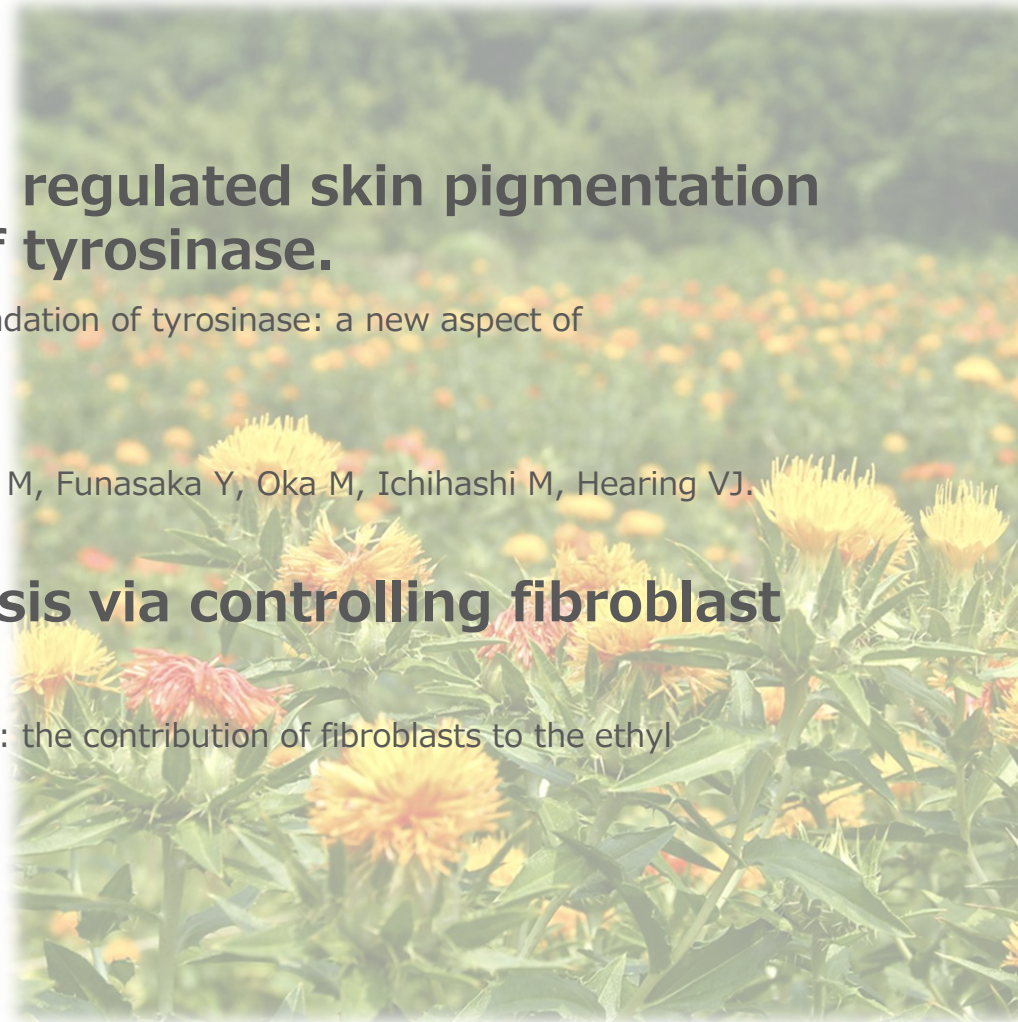
Ando H, Watabe H, Valencia JC, Yasumoto K, Furumura M, Funasaka Y, Oka M, Ichihashi M, Hearing VJ.

- ✓ **VF-LINO suppress melanogenesis via controlling fibroblast derived signals.**

Interactions between melanocytes and neighboring cells: the contribution of fibroblasts to the ethyl linoleate-induced inhibition of melanogenesis

IPCC Conference 2017

Yokota M, Yoshimoto S, Yoshida M, Yahagi S, Ando H



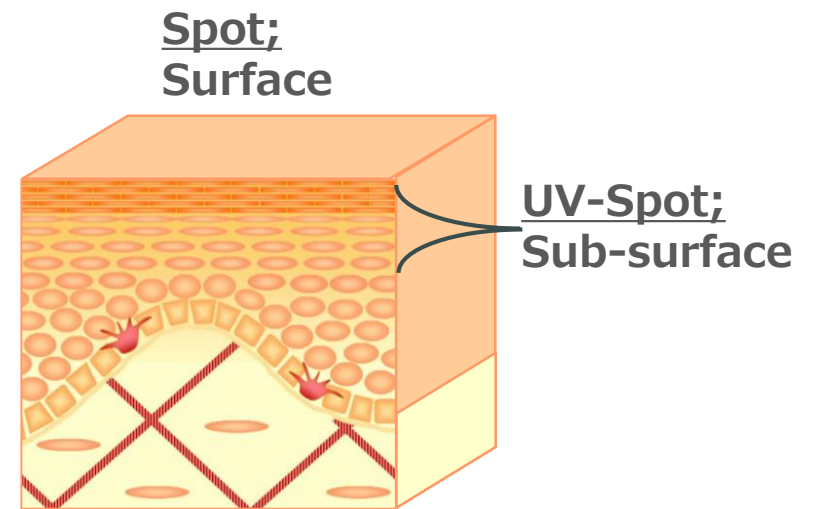
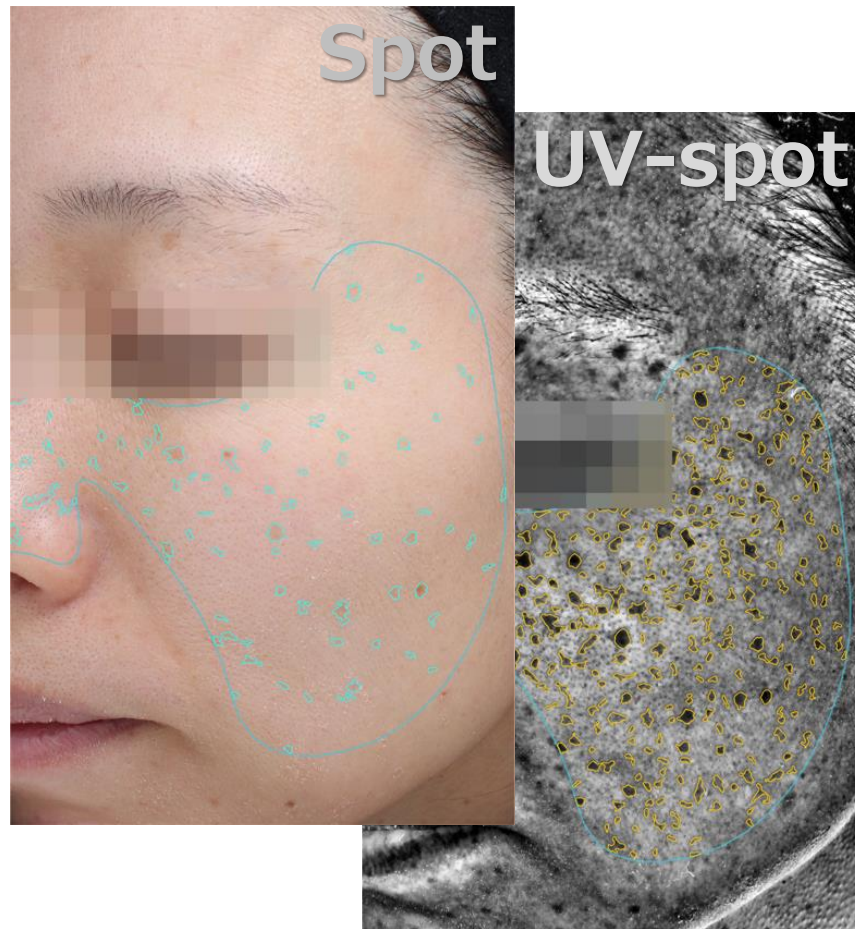
Test profile & Methods

Lists	Contents
Test sample	-2% VF-LINO cream -Placebo cream
Number of subjects	-21 (PIH patients, female, age20~55)
Test region	-Face
Treatment	-Twice a day <i>Both samples were treated to half face with blind</i>
Term	-Total 4 weeks <i>Evaluate each 2 weeks</i>
Measurement	-VISIA-CR (Spot, UV-spot) -Physical measures <i>Skin color (L^*), SC area using iScope (pixel)</i> -Questionnaire

Test formulation

INCI	Placebo	2% Ethyl linolate
Cetheth-20	1.00	1.00
Sorbeth-40 Tetraoleate	0.50	0.50
Glyceryl Stearate	1.00	1.00
Cetyl Alcohol	5.00	5.00
Squalane	10.00	10.00
Isocetyl Myristate	6.00	6.00
Triethylhexanoin	3.00	3.00
Simmondsia Chinensis (Jojoba) Seed Oil	1.00	1.00
Dimethicone	0.20	0.20
Ethyl linolate	0.00	2.00
Propyl paraben	0.10	0.10
Methyl paraben	0.20	0.20
Butylene glycol	5.00	5.00
Xanthan Gum	0.10	0.10
Water	66.90	64.90
Total	100.00	100.00

Test profile & Methods



Spot and UV-Spot related to PIH were decreased significantly after 4 weeks treatment of VF-LINO.

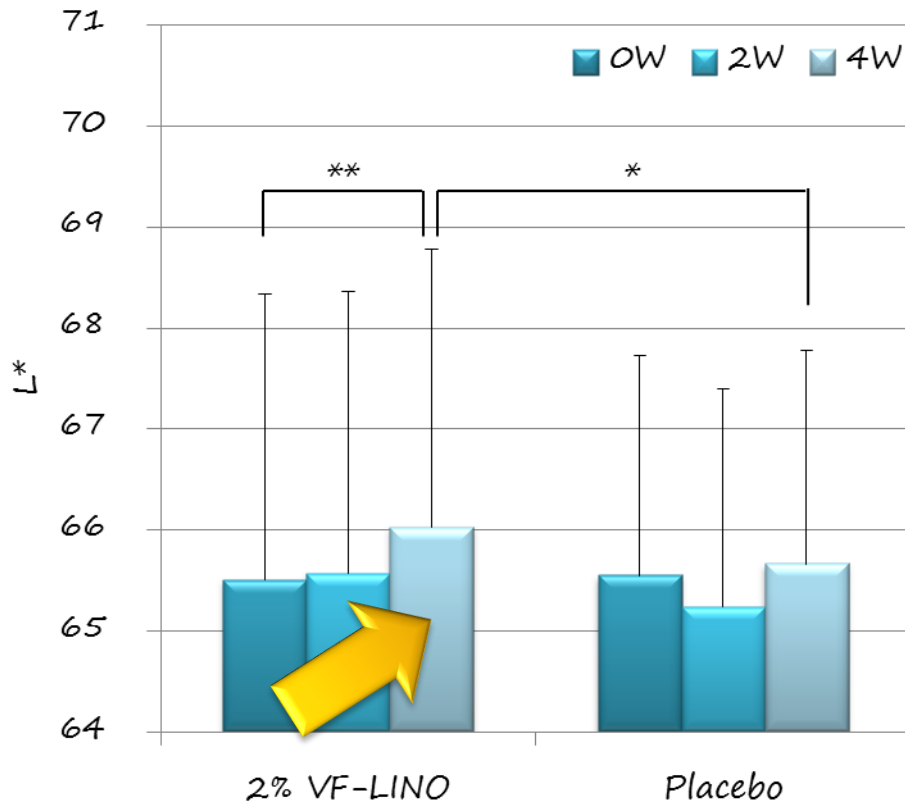
		2% VF-LINO cream			Placebo cream		
		0W	2W	4W	0W	2W	4W
Measurement value	Spot	0.032 ± 0.028	0.020 ± 0.015	0.014 ± 0.009	0.025 ± 0.025	0.030 ± 0.028	0.023 ± 0.024
	UV-Spot	69.559 ± 18.817	65.819 ± 19.380	67.337 ± 18.497	64.040 ± 18.207	62.033 ± 18.899	63.903 ± 17.664
Significance vs. 0W	Spot			***			
	UV-Spot		***	*		*	
Significance vs. Placebo	Spot		****	*****			
	UV-Spot		*	*			

Significance (ANOVA Contrast test); $p^* < 0.05$, $p^{**} < 0.01$, $p^{***} < 0.001$
Significance (Wilcoxon's signed rank test); $p^{****} < 0.025$, $p^{*****} < 0.0005$

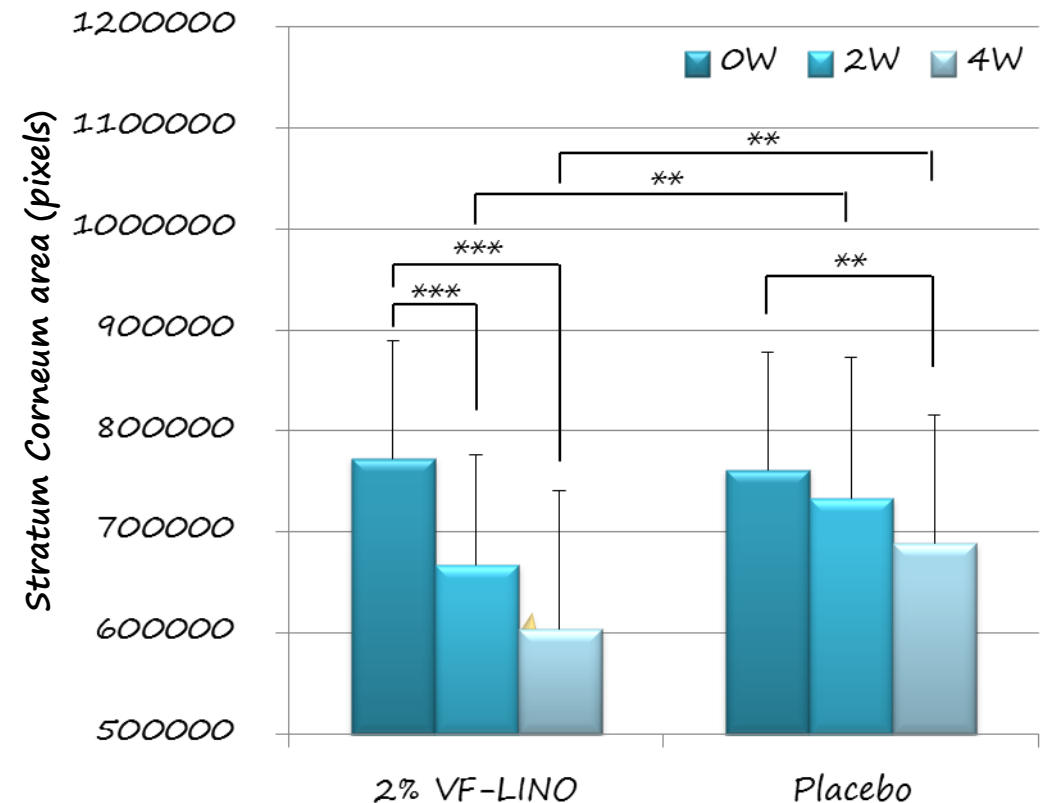
L* increase and SC area decrease following to the turnover promotion were observed significantly after 4 weeks treatment of VF-LINO.

Results of physical measurement

Skin color



SC area



Significance (ANOVA Contrast test); $p < 0.05$, $p^{**} < 0.01$, $p^{***} < 0.001$

Skin color of whole face was brighten, moreover PIH were recovered after 4 weeks treatment of VF-LINO.

Representative photos of PIH recovery



Conclusion of VF-LINO

	VF-LINO	Placebo
Spot	↓ ***	→
UV-Spot	↓ *	→
Skin color	↑ **	→
Skin turnover	↑ ***	↑ **

VF-LINO recovered PIH remarkably so as all parameters changed positive indicated in yellow.

Appendix of VF-LINO

Evaluation of melanin production after 6 days cultivation.



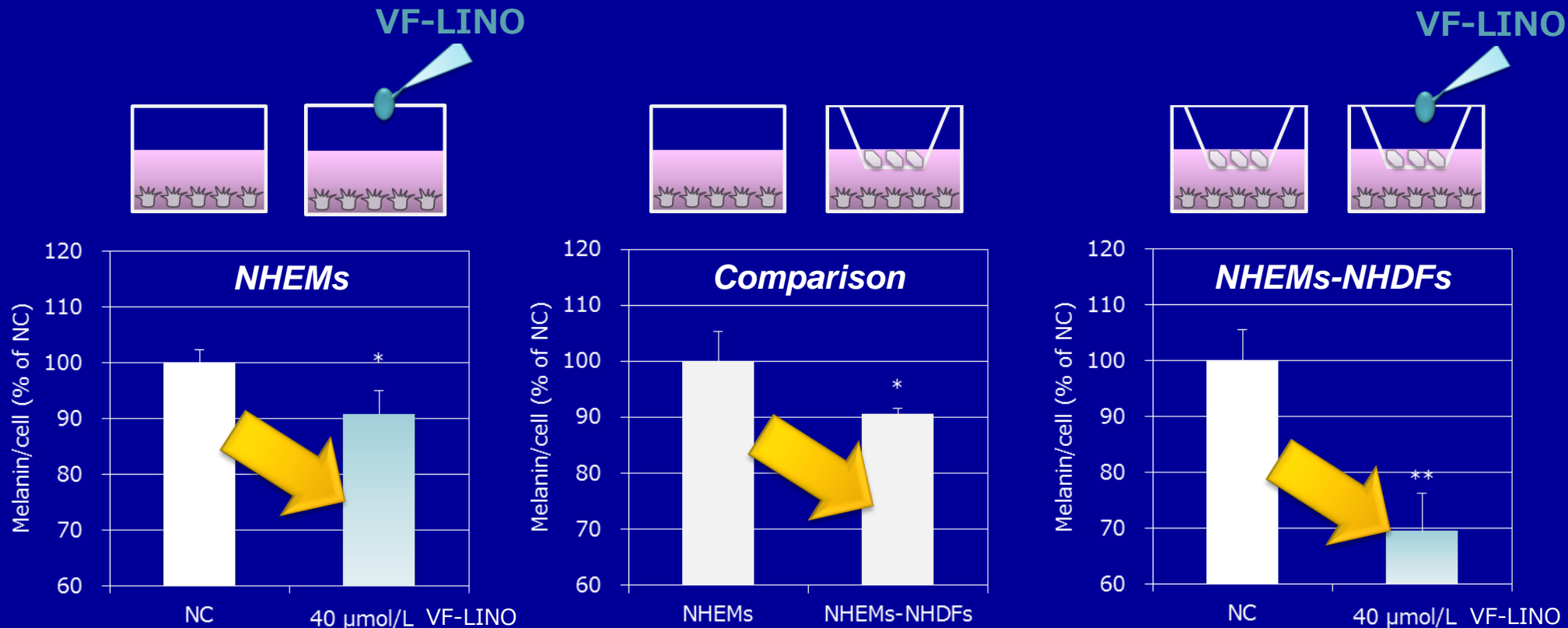
MSF types		RHEEs (NHEM derived by Caucasian)		RHEEs (NHEM derived By African American)	
α MSH	ET-1	NC	VF-LINO	NC	VF-LINO
—	—				
100 nmol/L	—				
—	10 nmol/L				



VF-LINO suppressed melanogenesis for both racial types

Appendix of VF-LINO

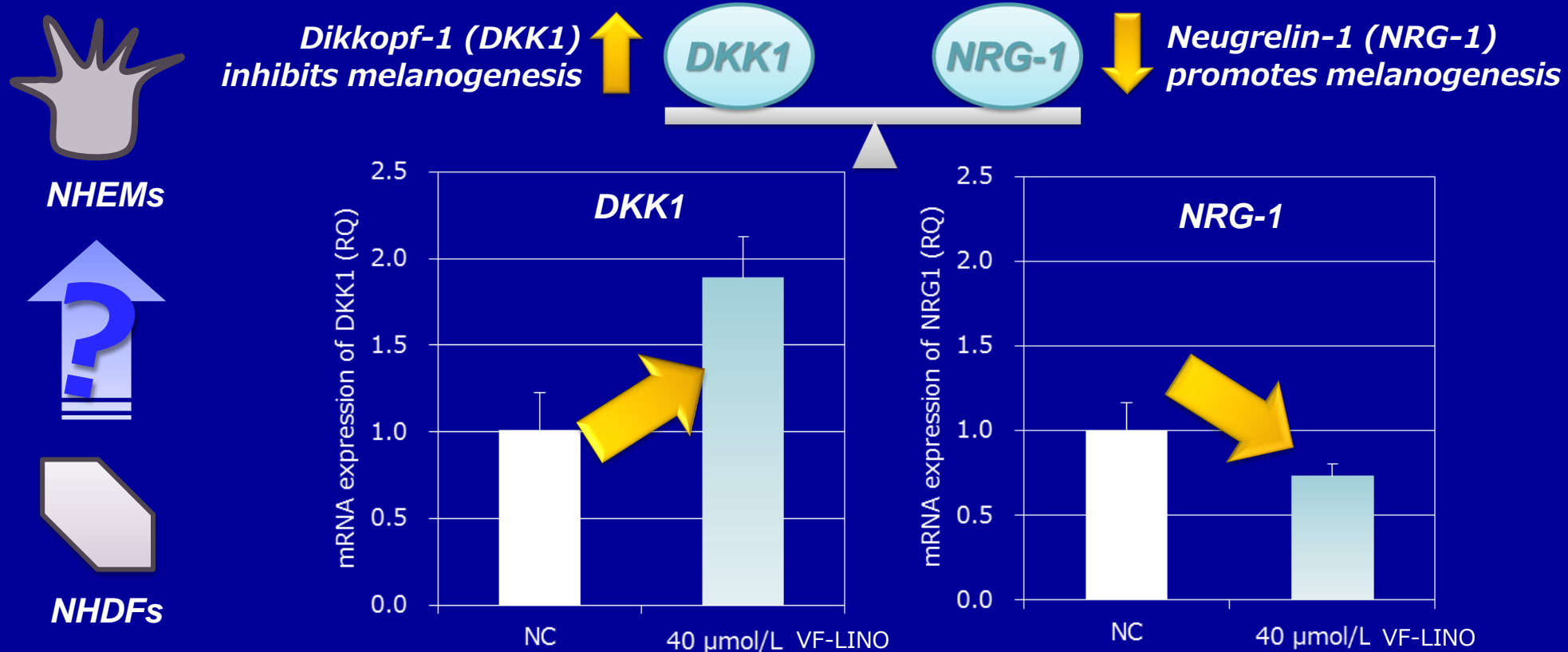
Evaluation of melanin production in co-culture model (NHEMs-NHDFs)



We observed that a healthy fibroblast can suppress melanogenesis. Adding VF-LINO on a co-culture model increases this suppression effect.

Appendix of VF-LINO

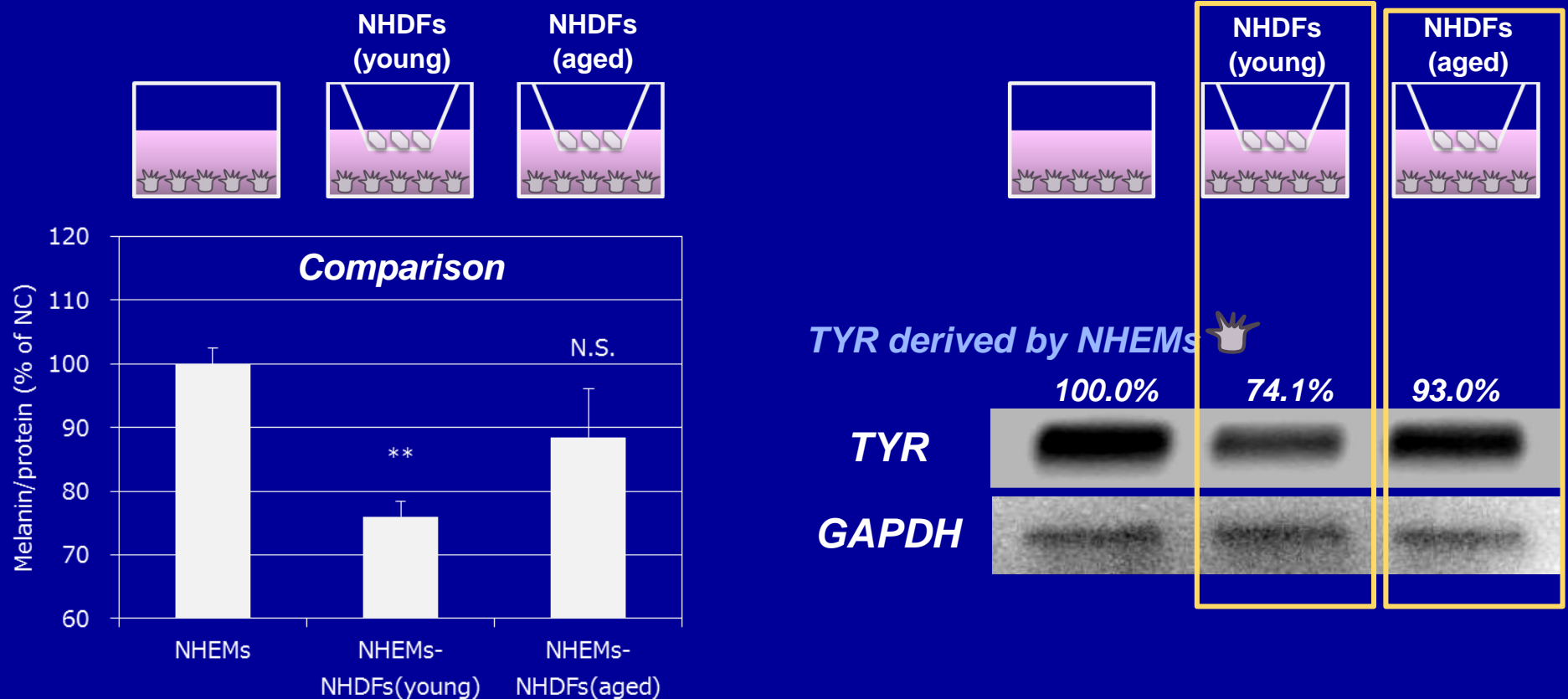
Evaluation of NHDFs derived melanocyte stimulating factor (MSF)



**VF-LINO regulated NHDFs derived MSF.
In fact, VF-LINO increased DKK1 and decreased NRG-1.**

Appendix of VF-LINO

Evaluation of melanin production after 6 days cultivation.



We have confirmed that melanogenesis suppression is weak when using an aged-fibroblast co-culture.